REMARKS

This document is submitted in response to the Office Action dated September 28, 2007 ("Office Action").

Upon entry of the proposed amendments, claims 1-3, 5-7, and 13-30 will be pending. Claims 4 and 8-12 have been canceled without prejudice. Applicants have amended claims 1-3, 5-7, 13 and 14, and added new claims 15-30. Support for the amendments and new claims can be found through out the specification, for example, at page 14, line 24 to page 15, line 11; page 16, line 8 to page 17, line 2; page 18, lines 9-28; page 19, line 35 to page 20, line 8; and page 28, lines 15-21. No new matter has been added.

Amendments to the Specification

The Office objected to the specification for containing an embedded hyperlink or other form of browser-executable code (See the Office Action, at page 2, paragraph 2).

Applicants have amended the specification to delete the hyperlink found on page 7, line 23, and respectfully request that this objection be withdrawn.

Information Disclosure Statement (IDS)

Applicants thank the Office for considering the references cited on the IDSs submitted on 12/14/05, 5/22/06, 6/20/06, 3/22/07, and 5/2/07. Applicants note that an IDS was submitted on 12/4/07 (after mailing of the present Office Action), and request that the Office consider the references cited therein.

35 U.S.C. § 101

The Office rejected claims 1-5 as allegedly directed to non-statutory subject matter. See the Office Action, at page 7, line 27 to page 8, line 8. Applicants have amended claims 1-3 and 5 to recite "isolated antibody" as suggested by the Office (see the Office Action, at page 7, lines 5-8). Claim 4 has been canceled. Therefore, withdrawal of this rejection is respectfully requested.

35 U.S.C. § 112, First Paragraph

The Office rejected claims 1-10, 13, and 14 as allegedly failing to comply with the enablement requirement on what appear to be four grounds. See the Office Action, at pages 4-7.

First, the Office asserted that, as the specification fails to disclose data demonstrating anti-PCI antibody activities *in vivo*, it fails to enable skilled practitioners to use such antibodies to treat or prevent disorders associated with hypercoagulation. See the Office Action, at page 4, lines 13-23. Applicants do not agree that the specification fails to enable such uses, or that *in vivo* data are required to enable these uses. However, for the sole purpose of moving this application forward, Applicants have canceled claims 4 and 8-10 and amended claims 13 and 14 to delete any recitation of these uses. Further, claims 1 and 3 have been amended to recite specific antibody sequences derived from certain anti-PCI antibodies described in the specification. As MPEP 2164.01(c) explains: "... when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use ... In other words, if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention." Thus, it is improper to reject claims that do not recite any therapeutic uses based on any alleged failure to enable therapeutic uses. As the Office acknowledges (see the Office Action, at page 4, lines 17-19), the specification discloses, among other things, *in vitro* data demonstrating that those anti-PCI antibodies having the recited sequences do indeed bind to PCI and inhibit PCI activities (see, e.g., at page 34, line 5, to page 35, line 10). Such data enable skilled practitioners to use the full scope of the claimed antibodies to, for example, detect PCI or inhibit PCI activities, and any one of these uses is more than sufficient to satisfy the enablement requirement.

As noted above, Applicants disagree that the specification fails to enable using the recited antibodies, compositions and kits to treat hypercoagulation-associated disorders. To this point, Applicants would like to address Fujita et al. (US 5,948,752, "Fujita") for the sake of clarifying the record. Fujita teaches that administration of PCI (purified from human urine) suppresses hypercoagulation in rats (see Example 3). Reading this, the Office concluded that administration

of anti-PCI antibodies would have an effect opposite to that disclosed in the specification (see the Office Action, at page 5, line 27 to page 6, line 9). However, at the time of filing, it was by no means accepted in the art that PCI has an anti-coagulant effect. In fact, Elisen et al (Blood, 1998, 91:1542-1547; "Elisen"), a reference cited in the Office Action (at page 8, line 17), teaches that PCI has been shown to be both an anti-coagulant and a pro-coagulant (see Elisen, Abstract). The authors of Elisen investigated this discrepancy, and ultimately concluded that PCI acts predominantly as a pro-coagulant in human plasma (see, e.g., Abstract, and page 1546, right column, last paragraph). Thus, the teaching of Elisen contradicts that of Fujita, and supports the disclosures of the instant application.

Second, the Office asserted that a claim reciting a composition for prevention of an disorder "encompasses 100% efficacy in 100% of patients" to whom the recited composition has been administered, and that the specification lacks data to show such 100% efficacy (see the Office Action, at page 5, lines 20-24). Applicants disagree with the Office's assertions about what would be required to establish enablement of a claim directed to prevention, and further point out that composition claims are considered enabled if any use is enabled. However, in view of the present amendments, the issue is moot.

Third, the Office contended that the instant claims read on "...variants and other antibodies that are 'functionally equivalent' to the antibodies recited by name or SEQ ID number ... 'functionally equivalent' read on mutant sequences comprising insertions, deletions, and substitutions, as well as sequences that are completely unrelated yet comprise the same biological activities (see the Office Action, at page 4, line 26 to page 5, line 19)." Applicants disagree with this contention, but since claims 1 and 3 have been amended to recite specific heavy chain and light chain CDR sequences for either the claimed antibody (claim 1) or the reference antibody (claim 3), and the term "functionally equivalent" does not appear in the present claims, the issue is moot.

Fourth, the Office suggested that a deposit of cell lines producing the antibodies is required to enable claim 3, which recites the antibodies PC19G8, PC23A7, PC23D8, PC30G1, PC31E2, PC31F1, and PC39C6. See the Office Action, at page 6, lines 10-17. Applicants have

amended claim 3 such that it no longer recites these particular antibodies, thus mooting this ground for rejection.

In view of the foregoing amendments and remarks, Applicants respectfully request that the Office reconsider and withdraw the rejection under 35 U.S.C. § 112, first paragraph.

35 U.S.C. § 102 (b)

The Office rejected claims 1-4 and 6 as allegedly anticipated by Meijers (Blood, 1988, 72:1401-1403, "Meijers") as evidenced by Elisen. Applicants disagree. However, for the purpose of expediting prosecution of this application, Applicants have amended claims 1 and 3 and canceled claim 4, and submit that Meijers does not anticipate any of the presently pending claims.

Meijers teaches anti-PCI monoclonal antibodies that inhibit PCI's ability to inhibit aPC activity in human plasma and *in vitro* (see, e.g., Abstract). Meijers does not show that these antibodies inhibit PCI's ability to inhibit the production of aPC by the thrombin /thrombomodulin (Thr/TM) complex (as acknowledged in the Office Action at page 9, lines 4-5). The reference also does not describe any structural information, e.g., CDR sequences or binding epitopes, for these antibodies.

Elisen teaches that PCI inhibits thrombin, and is predominantly a pro-coagulant in human plasma (see page 1546, right column, last paragraph).

Claim 1 is directed to an isolated anti-PCI antibody with a specific sequence for each of its heavy and lightchain CDRs. As noted above, Meijers does not disclose the sequence of any antibody. There is no reason to assume that the Meijers antibodies would have any of the CDR sequences recited in claim 1. Therefore, Meijers does not anticipate claim 1 or any of its dependent claims.

Claim 3 is directed to an isolated antibody that exhibits a specific PCI-inhibiting activity and competes for the same binding site as a reference antibody having a specified sequence for each of its heavy chain and light chain CDRs. Meijers does not provide any information that would lead a skilled practitioner to conclude anything about the epitope specificity of any of its

antibodies. The Office Action (at page 8, line 24 to page 9, line 1) appears to assume that, if two anti-PCI antibodies exhibit a similar activity, then they must bind to the same binding site on PCI. This is an unwarranted assumption. Even if two antibodies both inhibit the activity of a given target antigen, they may well bind to two distinct epitopes on the antigen. It cannot even be assumed that an anti-PCI antibody must bind to those PCI residues that interact with aPC in order to be able to disrupt PCI-aPC interactions. An anti-PCI antibody might, for example, bind to a site that is close to those residues, and by mere steric hindrance interfere with PCI-aPC interactions. One simply cannot conclude that Meijer's antibodies bind to the same site as any of the antibodies recited in claim 3. Thus, Meijers does not anticipate claim 3 or its dependent claims.

Furthermore, there is no scientific basis for the Office's assertion that the antibodies disclosed in Meijers must also inherently inhibit PCI's ability to inhibit the production of aPC by the Thr/TM complex, as evidenced by the teaching of Elisen. See the Office Action, at page 9, lines 4-22. The instant specification describes seven anti-PCI antibodies, all of which inhibit PCI's ability to inhibit aPC activity, but not all of which are also able to inhibit PCI's ability to inhibit the production of aPC by the Thr/TM complex (see Table 1). Clearly, these two activities do not always go together, and it is unreasonable to conclude that the antibodies disclosed in Meijers necessarily have both.

Accordingly, for at least the reasons set forth above, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. §102 (b).

35 U.S.C. § 103

The Office rejected claims 1, 2, and 5 as allegedly obvious over Meijers, further in view of Kovari et al. (Structure, 1995, 3:1291-3; "Kovari"). Applicants traverse.

As discussed above, Meijers does not disclose an antibody having the particular heavy chain and light chain CDR sequences recited in claim 1, as amended. In fact, the reference provides no information at all about anti-PCI antibody sequences. Thus, reading Meijers, a skilled practitioner would not have been led to an antibody having the recited CDR sequences.

Kovari, the secondary reference, does not rectify the deficiencies of Meijers. Kovari merely presents a review on the use of antibody fragments for crystallization and structure studies. There is absolutely nothing in Kovari to suggest an antibody with any of the CDR sequences recited in claim 1. Thus, even if skilled practitioners were to combine the teachings of Meijers and Kovari, they still would not have arrived at Applicants' antibodies. Claim 1, and claims 2 and 5 depending from it, are therefore not obvious over Meijers and Kovari.

Applicants respectfully request that the Office withdraw this rejection under 35 U.S.C. § 103.

CONCLUSION

Applicants respectfully submit that all pending claims are in condition for allowance, which action is expeditiously requested. Applicants do not concede any positions of the Examiner that are not expressly addressed above, nor do Applicants concede that there are not other good reasons for patentability of the presented claims or other claims. The fees in the amount of $1,880 for excess claims and $460 for a two-month extension of time is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Apply any other charges or credits to deposit account 06-1050, referencing Attorney's Docket No. 14875-147US1.

Respectfully submitted,

Date: February 28, 2008

/Janis K. Fraser/
Janis K. Fraser, Ph.D., J.D.
Reg. No. 34,819

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110
Telephone: (617) 542-5070
Facsimile: (617) 542-8906